

REMARKS/ARGUMENTS

Claims 45-47, 49, 50, 58, 59, 61 and 62 are currently under examination. Claims 48, 52-56, 63, 64 and 65 are currently withdrawn. Claims 45, 46 and 63-65 have been amended herein. Support for these amendments can be found in paragraphs [0037], [0130], Example 6 and original Claim 60. Claims 1-44, 51, 57, 60 and 66-75 have been cancelled without intending to abandon or to dedicate to the public any patentable subject matter.

Examiner Interview Summary

Applicant wishes to thank Examiner Lucas for the courtesy extended to Applicant's representative, Gary Connell, in conducting a personal interview on October 28, 2009, at which time the rejections previously imposed under 35 U.S.C. §112, first paragraph and 35 U.S.C. §102 were discussed, as well as proposed claim amendments. The amendments presented in this Amendment and Response are believed to be consistent with the amendments discussed at the interview to address the outstanding rejections.

Election/Restriction

The Examiner maintains the Restriction requirement arguing that the present claims are anticipated by WO'257 (PCT Publication No. WO 2003/068257). As noted below, Applicant contends that the present claims are not anticipated by this reference and therefore the pending claims are directed to a single invention and request the withdrawal of the Examiner's restriction of diagnostic claim 63.

Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected Claims 45-47, 49, 50, 58, 59, 61 and 62 under 35 U.S.C. § 112, first paragraph, as lacking enablement for any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the claimed invention. Applicant has amended independent claims 45, 46 and 63-65 to incorporate the limitations of Claim 60 as suggested by the Examiner. Therefore, Applicant submits that the Claims, as amended, are sufficiently enabled by the specification and request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

Claim Rejections Under 35 U.S.C. § 102

The Examiner has maintained the rejection of Claims 45-47, 49, 50 and 58-62 under 35 U.S.C. § 102(b) as being anticipated by WO'257 (PCT Publication No. WO 2003/068257). The Examiner initially agrees with Applicant's previous assertion that WO'257 does not teach the cycling of the immune system in a patient suffering from a disease characterized by the production of regulator cells. Nonetheless, the Examiner states that WO'257 teaches that "monitoring should be maintained for at least a month which would inherently detect the changes in the cycle." Furthermore, the Examiner contends that "the performance of the method described by the reference would inherently result in the monitoring of the immune system cycling, and the administration of anti-regulatory cell agents at the time point indicated by the present claims."

As discussed in detail below, Applicant disagrees with this rejection. Nonetheless, in an effort to expedite prosecution, Applicant has amended claims 45 and 46 to clarify that the monitoring of patient continues for at least one cycle of the immune system and that the analysis of the results from patient monitoring therefore results in understanding the dynamics of the immune system cycling. These amendments were discussed at the interview and are believed to address the concerns of the Examiner

Applicant disagrees with the Examiner's interpretation of the teachings of WO'257. Specifically, at page 12 lines 20 to 22, WO'257 teaches:

*"Optimally, the monitoring is continued to determine the effect of the agent. Insufficient ablation, **re-emergence** of the regulator cells or **increases** in tumour load will mean that the method of the present invention should be repeated.*
(emphasis added)

Applicant submits that a person of ordinary skill in the art, when reading this section of the cited document would immediately realize that the monitoring may be continued after the administration of the agent to see if the treatment has been effective (or to use the specific words in the cited document "to determine the effect of the agent"). If there is evidence that the desired effect has not been achieved, the prior art teaches that the method should be repeated, namely the immune system "reset" and the patient then monitored for re-emerging regulator cells. In other words, WO'257 clearly teaches that monitoring is only continued to the point where it is

determined that the treatment may have been ineffective.

There is no suggestion in WO'257 that monitoring is to be continued once it is detected that treatment was not effective. Any further monitoring would only occur after a further resetting of the immune system. As a result, contrary to the Examiner's assertions, there is no way the skilled person would inherently identify immune system cycling because there is no instruction in WO'257 to continue monitoring for a significant length of time for there to be any chance that the immune system cycling could be detected.

Thus, WO'257 can be considered to teach the following steps:

- a) resetting the immune system in the patient,
- b) monitoring the patient so that regulator cells that clonally expand immediately following resetting are detected,
- c) administering the agent to reduce the activity and/or production of regulator cells that are clonally expanding,
- d) monitoring the patient for a sufficient length of time, for example at least a month, to determine if the treatment has been effective, and
- e) as soon as (and if) there is evidence the treatment has not been effective, for example by detecting an increase in tumor load, stop monitoring and preferably repeat the procedure starting with resetting the immune system in the patient.

The period of a month for continued monitoring noted by the Examiner is simply to provide the patient with confidence that the treatment has been effective. If the monitoring shows that the therapy has been effective, there will be no opportunity to observe cycling. Alternatively, if the administered therapy has not been effective, WO'257 clearly indicates that monitoring is stopped and the treatment procedure is repeated, and thus there will be no opportunity to detect cycling.

The Examples of WO'257 also confirm these observations regarding monitoring the patient following the resetting and treatment. In each instance, the skilled artisan would appreciate that WO'257 teaches that the patient is monitored to determine whether the treatment has been effective, and if there is evidence that the treatment has not been effective, the monitoring is to be stopped and preferably the procedure (as outlined above) repeated.

The standard for inherent anticipation is quite clear. While inherent or implicit

disclosures within references may be used to support rejections under 35 U.S.C. § 102, “the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.” MPEP § 2112 (IV) (citing *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993)) (emphasis in original). “Inherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

Thus, when a claim limitation is not explicitly set forth in a reference, the extrinsic evidence must make clear that the characteristic is necessarily and inevitably present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). It is not sufficient if a material element or limitation is “merely probably or possibly present” in the prior art. *Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 1295 (Fed. Cir. 2002). Additionally, anticipation “cannot be predicated on mere conjecture respecting the characteristics of products that might result from the practice of processes disclosed in references.” *W.L. Gore v. Garlock, Inc.*, 721 F.2d at 1554 (Fed. Cir. 1983). Inherency, therefore, may not be established by probabilities or possibilities, but only by a characteristic that is always present in a product or occurs each and every time a process is carried out. *Robertson, supra*, at 1950-51. The burden falls on the Examiner to provide a basis in fact and/or technical reasoning to support the assertion that the inherent property necessarily flows from the prior art. *Ex Parte Levy*, 17 USPQ.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

Thus, in this case it is incumbent upon the Examiner to provide a factual basis for the argument that the skilled artisan would necessarily and inevitably detect and discover immune system cycling following a resetting of the immune system through the administration of an agent that inhibits the production of, limits the function of, and/or destroys, regulator cells. And it is insufficient in the instant case for the Examiner to cite an example of an administration of such an agent followed by monitoring designed to assess the efficacy of the therapy, and conjecture that it is merely possible or probable that the monitoring will result in recognition of immune system cycling.

As explained above, not only does WO’257 not teach cycling, as stated by the Examiner,

it does not teach or suggest that the skilled person continue monitoring for a sufficient length of time to detect immune system cycling if the treatment has been ineffective. Furthermore, the Examiner's rejection is based on an assumption that the detection of immune system cycling would necessarily occur when the monitoring is conducted for a period of about a month. In this regard, there is no guarantee that the skilled artisan would detect immune system cycling in patients in which treatment has not been effective. More specifically, review of various data points of various levels over time from biological samples does not indicate that the skilled artisan would automatically observe cycling. Given the standard variation in biological sampling, Applicant submits that it is very unlikely that immune cycling would be detected unless the skilled artisan knew in advance that cycling should be occurring. This understanding is only found in the instant disclosure and it is improper hindsight analysis for the Examiner to argue that the teachings in Applicant's disclosure would inherently be realized when the cited prior art makes clear that such recognition did not, in fact, take place.

In conclusion, the Examiner's assertions contradict the teachings of the cited art and even if the Examiner's statements were correct, they improperly rely on assumptions about what a skilled artisan might inherently understand from the cited reference, as opposed to what is actually taught in the cited art. Thus, Applicant submits that the pending claims are not inherently anticipated by WO'257, and respectfully request that this objection under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Double Patenting

The Examiner has maintained the rejection of Claims 45-47, 49, 50 and 58-62 as being unpatentable over claims 26-28, 31, 32, 35, 36-38 and 42-47 of co-pending U.S. Patent Application No. 10/503,794.

The Examiner has also maintained the rejection of Claims 45-47, 49, 50 and 58-62 as being unpatentable over claims 1-4, 6, 10-13 and 15 of copending U.S. Patent Application No. 12/333,369.

Applicant respectfully submits that these provisional obviousness-type double patenting rejections will be addressed at such time that claims of the instant application or the co-pending patent applications cited by the Examiner have been found allowable. As this is not currently the

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status of any claims in the instant or the co-pending patent applications, Applicant requests that this rejection be held in abeyance.

Based upon the foregoing, Applicant believes that all pending claims are in condition for allowance and such disposition is respectfully requested. In the event that a telephone conversation would further prosecution and/or expedite allowance, the Examiner is invited to contact the undersigned.

Respectfully submitted,
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